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=> FIL MEDLINE BIOSIS SCISEARCH EMBASE CA
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=> s ribozym?
L1         25039 RIBOZYM?

=> s s trna
L2           147 S TRNA

=> s trna
L3         91919 TRNA

=> s l1 (5n) (link? or conjugat? or bound? or bond? or bind?) (5n) l3
L4            39 L1 (5N) (LINK? OR CONJUGAT? OR BOUND? OR BOND? OR BIND?) (5N)
                 L3

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5            16 DUP REM L4 (23 DUPLICATES REMOVED)

=> s l5 and py<=2000
<------User Break------>

SEARCH ENDED BY USER

=> s l1 (5n) (link? or conjugat? or bound? or bond? or bind? or attach?) (5n) l3
L6            41 L1 (5N) (LINK? OR CONJUGAT? OR BOUND? OR BOND? OR BIND? OR ATTAC
                 H?) (5N) L3

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7            16 DUP REM L6 (25 DUPLICATES REMOVED)

=> s l7 and py<=2000
   2 FILES SEARCHED...
L8            11 L7 AND PY<=2000

=> d l8 ibib abs 1-11

L8   ANSWER 1 OF 11      MEDLINE on STN
ACCESSION NUMBER:    1999435736      MEDLINE
DOCUMENT NUMBER:     PubMed ID: 10504232
TITLE:               The track of the pre-tRNA 5' leader in the ribonuclease P
```

ribozyme-substrate complex.
AUTHOR: Christian E L; Harris M E
CORPORATE SOURCE: Center for RNA Molecular Biology, Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106, USA.
CONTRACT NUMBER: GM56740 (NIGMS)
SOURCE: Biochemistry, **(1999 Sep 28)** 38 (39) 12629-38.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991020

AB The ribonuclease P (RNase P) **ribozyme** is an endonuclease that **binds** precursor **tRNAs** and catalyzes the removal of 5' leader nucleotides. Biochemical and photo-cross-linking studies have identified sites of contact between the mature tRNA domain of pre-tRNA and the ribozyme; however, relatively little is known about the location of the 5' leader in the ribozyme-substrate complex. To investigate the local three-dimensional environment of the 5' leader, we employed the short-range photo-cross-linking agent 4-thiouridine (s(4)U). The s(4)U photoagent was incorporated into a series of pre-tRNA substrates containing unique uridine residues in the 5' leader sequence at positions -1, -3, -5, -7, or -10. The modified substrates formed high-affinity complexes with the ribozyme and produced discrete intermolecular cross-links to RNase P RNA from Bacillus subtilis. Locations of the cross-**linked** nucleotides in the **ribozyme** and pre-**tRNA** were determined by reverse transcriptase primer extension. Photoagents incorporated into the 5' leader detected discrete elements of ribozyme structure in a progression from J18/2 to L15 to P3. Importantly, all of the cross-linked species retained the ability to cleave the covalently attached pre-tRNA, indicating that the cross-links reflect the native structure of the ribozyme-substrate complex. Together with available structural and biochemical data, the cross-linking results suggest a model for the position of the 5' leader within the ground-state ribozyme-substrate complex.

L8 ANSWER 2 OF 11 MEDLINE on STN
ACCESSION NUMBER: 1999177335 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10076002
TITLE: Design, characterization and testing of tRNA3Lys-based hammerhead ribozymes.
AUTHOR: Medina M F; Joshi S
CORPORATE SOURCE: Department of Medical Genetics and Microbiology, Faculty of Medicine, University of Toronto, 150 College Street #212, Toronto, Ontario M5S 3E2, Canada.
SOURCE: Nucleic acids research, **(1999 Apr 1)** 27 (7) 1698-708.
Journal code: 0411011. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990609

AB A hammerhead ribozyme targeted against the HIV-1 env coding region was expressed as part of the anticodon loop of human tRNA3Lys without sacrificing tRNA stability or ribozyme catalytic activity. These

tRNA-ribozymes were isolated from a library which was designed to contain linkers (sequences connecting the ribozyme to the anticodon loop) of random sequence and variable length. The ribozyme target site was provided in cis during selection and in trans during subsequent characterization. **tRNA-ribozymes** that possessed ideal combinations of **linkers** were expected to recognize the cis target site more freely and undergo cleavage. The cleaved molecules were isolated, cloned and characterized. Active tRNA-ribozymes were identified and the structural features conducive to cleavage were defined. The selected tRNA-ribozymes were stable, possessed cleavage rates lower or similar to the linear hammerhead ribozyme, and could be transcribed by an extract containing RNA polymerase III. Retroviral vectors expressing tRNA-ribozymes were tested in a human CD4+ T cell line and were shown to inhibit HIV-1 replication. These tRNA3Lys-based hammerhead ribozymes should therefore prove to be valuable for both basic and applied research. Special application is sought in HIV-1 or HIV-2 gene therapy.

L8 ANSWER 3 OF 11 MEDLINE on STN
ACCESSION NUMBER: 1999152377 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10026268
TITLE: Identification of adenosine functional groups involved in substrate binding by the ribonuclease P ribozyme.
AUTHOR: Siew D; Zahler N H; Cassano A G; Strobel S A; Harris M E
CORPORATE SOURCE: Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106, USA.
CONTRACT NUMBER: GM56740 (NIGMS)
SOURCE: Biochemistry, **(1999 Feb 9)** 38 (6) 1873-83.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990316
Last Updated on STN: 19990316
Entered Medline: 19990304

AB The RNA component of bacterial ribonuclease P (RNase P) binds to substrate pre-tRNAs with high affinity and catalyzes site-specific phosphodiester bond hydrolysis to generate the mature tRNA 5' end. Herein we describe the use of biotinylated pre-tRNA substrates to isolate RNase P ribozyme-substrate complexes for nucleotide analogue interference mapping of ribozyme base functional groups involved in substrate recognition. By using a series of adenosine base analogues tagged with phosphorothioate substitutions, we identify specific chemical groups involved in substrate binding. Only 10 adenosines in the Escherichia coli ribozyme show significant sensitivity to interference: A65, A66, A136, A232-234, A248, A249, A334, and A347. Most of these adenosine positions are universally conserved among all bacterial RNase P RNAs; however, not all conserved adenosines are sensitive to analogue substitution. Importantly, all but one of the sensitive nucleotides are located at positions of intermolecular cross-linking between the ribozyme and the substrate. One site of interference that did not correlate with available structural data involved A136 in J11/12. To confirm the generality of the results, we repeated the interference analysis of J11/12 in the Bacillus subtilis RNase P ribozyme, which differs significantly in overall secondary structure. Notably, the B. subtilis ribozyme shows an identical interference pattern at the position (A191) that is homologous to A136. Furthermore, mutation of A136 in the E. coli ribozyme gives rise to a measurable increase in the equilibrium binding constant for the ribozyme-substrate interaction, while mutation of a nearby conserved nucleotide (A132) that is not sensitive to analogue incorporation does not. These results strongly support direct participation of nucleotides

in the P4, P11, J5/15, and J18/2 regions of **ribozyme** structure in pre-**tRNA binding** and implicate an additional region, J11/12, as involved in substrate recognition. In aggregate, the interference results provide a detailed chemical picture of how the conserved nucleotides adjacent to the pre-tRNA substrate contribute to substrate binding and provide a framework for subsequent identification of the specific roles of these chemical groups in substrate recognition.

L8 ANSWER 4 OF 11 MEDLINE on STN
ACCESSION NUMBER: 1999080176 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9860878
TITLE: Identification of individual nucleotides in the bacterial ribonuclease P ribozyme adjacent to the pre-tRNA cleavage site by short-range photo-cross-linking.
AUTHOR: Christian E L; McPheeters D S; Harris M E
CORPORATE SOURCE: Center for RNA Molecular Biology, Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106, USA.
CONTRACT NUMBER: AI09293 (NIAID)
GM52310 (NIGMS)
GM56740 (NIGMS)
SOURCE: Biochemistry, **(1998 Dec 15)** 37 (50) 17618-28.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 19990128
Entered Medline: 19990114

AB The bacterial RNase P ribozyme is a site-specific endonuclease that catalyzes the removal of pre-tRNA leader sequences to form the 5' end of mature tRNA. While several specific interactions between enzyme and substrate that direct this process have been determined, nucleotides on the ribozyme that interact directly with functional groups at the cleavage site are not well-defined. To identify individual nucleotides in the ribozyme that are in close proximity to the pre-tRNA cleavage site, we introduced the short-range photoaffinity cross-linking reagent 6-thioguanosine (s6G) at position +1 of tRNA and position -1 in a tRNA bearing a one-nucleotide leader sequence [tRNA(G-1)] and examined cross-linking in representatives of the two structural classes of bacterial RNase P RNA (from Escherichia coli and Bacillus subtilis). These photoagent-modified tRNAs bind with similar high affinity to both ribozymes, and the substrate bearing a single s6G upstream of the cleavage (-1) site is cleaved accurately. Interestingly, s6G at position +1 of tRNA cross-links with high efficiency to homologous positions in J5/15 in both E. coli and B. subtilis RNase P RNAs, while s6G at position -1 of tRNA(G-1) cross-links to homologous nucleotides in J18/2. Both cross-links are detected over a range of ribozyme and substrate concentrations, and importantly, **ribozymes** cross-**linked** to position -1 of **tRNA**(G-1) accurately cleave the covalently attached substrate. These data indicate that the conserved guanosine at the 5' end of tRNA is adjacent to A248 (E. coli) of J5/15, while the base upstream of the substrate phosphate is adjacent to G332 (E. coli) of J18/2 and, along with available biochemical data, suggest that these nucleotides play a direct role in binding the substrate at the cleavage site.

L8 ANSWER 5 OF 11 MEDLINE on STN
ACCESSION NUMBER: 1998332319 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9669656
TITLE: Virion encapsidation of tRNA(3Lys)-ribozyme chimeric RNAs inhibits HIV infection.

AUTHOR: Westaway S K; Cagnon L; Chang Z; Li S; Li H; Larson G P; Zaia J A; Rossi J J
CORPORATE SOURCE: Department of Molecular Biology, Beckman Research Institute of the City of Hope, Duarte, California 91010-3011, USA.
CONTRACT NUMBER: AI25959 (NIAID)
AI29329 (NIAID)
SOURCE: Antisense & nucleic acid drug development, **(1998 Jun)** 8 (3) 185-97.
Journal code: 9606142. ISSN: 1087-2906.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980925
Last Updated on STN: 19980925
Entered Medline: 19980917

AB Retroviruses require a specific host cellular tRNA primer for initiation of first-strand DNA synthesis. This primer is bound by viral proteins and copackaged into virions. We have exploited this property in the design and testing of an antiviral ribozyme fused to tRNA(3Lys), the primer used for lentiviral replication, including human immunodeficiency virus (HIV-1 and HIV-2). The chimera consists of **tRNA**(3Lys) covalently **attached** to a hammerhead **ribozyme**, which is targeted to the region immediately upstream of the primer binding site of the HIV-1 genome. The tRNA-ribozyme chimeric transcript is catalytically active in vitro and is efficiently bound by HIV reverse transcriptase with an affinity similar to that of tRNA(3Lys). We have expressed the chimeric RNAs from either the tRNA(3Lys) intragenic RNA polymerase III promoter or from a human U6 snRNA promoter. The U6 promoter results in up to 10-fold enhanced expression of the tRNA-ribozyme. Most importantly, the tRNA(3Lys)-ribozymes are encapsidated in HIV-1 virions such that they are effective in substantially reducing the level of infectious virus produced from cells cotransfected with HIV-1 proviral DNA. These results demonstrate the feasibility of using this novel strategy to reduce HIV infectivity and more generally indicate the potential power of using the retroviral primer tRNAs as tools for expressing and delivering ribozymes and other antiretroviral RNAs to the virion capsid.

L8 ANSWER 6 OF 11 MEDLINE on STN
ACCESSION NUMBER: 87276580 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2440726
TITLE: Similarities between a predicted secondary structure for the M1 RNA **ribozyme** and the **tRNA** **binding** center of 16 S rRNA from E. coli.
AUTHOR: Boehm S
SOURCE: FEBS letters, **(1987 Aug 17)** 220 (2) 283-7.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198709
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19870923

AB We propose a new model for the secondary structure of the M1 RNA component of E. coli RNase P which is based on significant sequence homologies with parts of the E. coli 16 S rRNA. A large domain of the new model resembles closely the secondary structure of the tRNA binding center of 16 S rRNA. We suggest that this domain of M1 RNA when functioning as a ribozyme binds the mature part of the precursor tRNA.

L8 ANSWER 7 OF 11 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:778962 SCISEARCH
THE GENUINE ARTICLE: 362LR
TITLE: Approaching translation at atomic resolution
AUTHOR: Puglisi J D (Reprint); Blanchard S C; Green R
CORPORATE SOURCE: STANFORD UNIV, SCH MED, DEPT BIOL STRUCT, STANFORD, CA 94305 (Reprint); JOHNS HOPKINS UNIV, SCH MED, HOWARD HUGHES MED INST, BALTIMORE, MD 21205; JOHNS HOPKINS UNIV, SCH MED, DEPT MOL BIOL & GENET, BALTIMORE, MD 21205
COUNTRY OF AUTHOR: USA
SOURCE: NATURE STRUCTURAL BIOLOGY, (**OCT 2000**) Vol. 7, No. 10, pp. 855-861.
Publisher: NATURE AMERICA INC, 345 PARK AVE SOUTH, NEW YORK, NY 10010-1707.
ISSN: 1072-8368.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 57

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Atomic resolution structures of 50S and 30S ribosomal particles have recently been solved by X-ray diffraction. These ribosomal structures show often unusual folds of ribosomal RNAs and proteins, and provide molecular explanations for fundamental aspects of translation. In the 50S structure, the active site for peptide bond formation was localized and found to consist of RNA. The ribosome is thus a **ribozyme**. In the 30S structures. **tRNA binding** sites were located. and molecular mechanisms for ribosomal fidelity were proposed. The 30S subunit particle has three globular domains, and relative movements of these domains may be required for translocation of the ribosome during protein synthesis. The structures are consistent with and rationalize decades of biochemical analysis of translation and usher in a molecular age in understanding the ribosome.

L8 ANSWER 8 OF 11 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:946461 SCISEARCH
THE GENUINE ARTICLE: 261WM
TITLE: Nuclease footprint analyses of the interactions between RNase P ribozyme and a model mRNA substrate
AUTHOR: Trang P; Hsu A W; Liu F Y (Reprint)
CORPORATE SOURCE: UNIV CALIF BERKELEY, SCH PUBL HLTH, PROGRAM INFECT DIS & IMMUN, 140 WARREN HALL, BERKELEY, CA 94720 (Reprint); UNIV CALIF BERKELEY, SCH PUBL HLTH, PROGRAM INFECT DIS & IMMUN, BERKELEY, CA 94720; UNIV CALIF BERKELEY, SCH PUBL HLTH, PROGRAM COMPARAT BIOCHEM, BERKELEY, CA 94720
COUNTRY OF AUTHOR: USA
SOURCE: NUCLEIC ACIDS RESEARCH, (**1 DEC 1999**) Vol. 27, No. 23, pp. 4590-4597.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 0305-1048.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 46

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB RNase P ribozyme cleaves an RNA helix substrate which resembles the acceptor stem and T-stem structures of its natural **tRNA** substrate. By **linking** the **ribozyme** covalently to a sequence (guide sequence) complementary to a target RNA, the catalytic RNA can be converted into a sequence-specific ribozyme, M1GS RNA, We have

previously shown that M1GS RNA can efficiently cleave the mRNA sequence encoding thymidine kinase (TK) of herpes simplex virus 1. In this study, a footprint procedure using different nucleases was carried out to map the regions of a M1GS ribozyme that potentially interact with the TK mRNA substrate. The ribozyme regions that are protected from nuclease degradation in the presence of the TK mRNA substrate include those that interact with the acceptor stem and T-stem, the 3' terminal CCA sequence and the cleavage site of a tRNA substrate. However, some of the protected regions (e.g. P13 and P14) are unique and not among those protected in the presence of a tRNA substrate. Identification of the regions that interact with a mRNA substrate will allow us to study how M1GS RNA recognizes a mRNA substrate and facilitate the development of mRNA-cleaving ribozymes for gene-targeting applications.

L8 ANSWER 9 OF 11 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:347977 CA
TITLE: Singly and Bifurcated Hydrogen-bonded Base-pairs in tRNA Anticodon Hairpins and Ribozymes
AUTHOR(S): Auffinger, Pascal; Westhof, Eric
CORPORATE SOURCE: Modelisations et Simulations des Acides Nucleiques, UPR 9002, Institut de Biologie Moleculaire et Cellulaire du CNRS, Strasbourg, 67084, Fr.
SOURCE: Journal of Molecular Biology (**1999**), 292(3), 467-483
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The tRNA anticodon loops always comprise seven nucleotides and is involved in many recognition processes with proteins and RNA fragments. We have investigated the nature and the possible interactions between the first (32) and last (38) residues of the loop on the basis of the available sequences and crystal structures. The data demonstrate the conservation of a bifurcated hydrogen bond interaction between residues 32 and 38, located at the stem/loop junction. This interaction leads to the formation of a non-canonical base-pair which is preserved in the known crystal structures of tRNA/synthetase complexes. Among the tRNA and tDNA sequences, 93 % of the 32·38 oppositions can be assigned to two families of isosteric base-pairs, one with a large (86 %) and the other with a much smaller (7 %) population. The remainder (7 %) of the oppositions have been assigned to a third family due to the lack of evidence for assigning them into the first two sets. In all families, the Y32·R38 base-pairs are not isosteric upon reversal (like the sheared G·A or wobble G·U pairs), explaining the strong conservation of a pyrimidine at position 32. Thus, the 32·38 interaction extends the sequence signature of the anticodon loop beyond the conserved U-turn at position 33 and the usually modified purine at position 37. A comparison with other loops containing both a singly hydrogen-bonded base-pair and a U-turn suggests that the 32·38 pair could be involved in the formation of a base triple with a residue in a rRNA component. It is also observed that two crystal structures of ribozymes (hammerhead and leadzyme) present similar base-pairs at the cleavage site. (c) 1999 Academic Press.

REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 11 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 123:189658 CA
TITLE: In vitro evolution of a self-alkylating ribozyme
AUTHOR(S): Wilson, Charles; Szostak, Jack W.
CORPORATE SOURCE: Dep. Molecular Biology, Massachusetts General Hospital, Boston, MA, 02114, USA
SOURCE: Nature (London) (**1995**), 374(6525), 777-82

CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English

AB RNA enzymes are postulated to have catalyzed all chemical reactions in the earliest living cells. This idea is now investigated in a search for alkyl transferases from a pool of random sequence RNAs. Selection for self-biotinylation yields a **tRNA**-like **ribozyme** that efficiently catalyzes carbon-nitrogen **bond** formation. Ribozymes can thus promote reactions other than those involving the RNA sugar-phosphate backbone, suggesting that RNA may be capable of a broad range of catalytic activities.

L8 ANSWER 11 OF 11 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 121:224845 CA
TITLE: Rational Design of Self-Cleaving pre-tRNA-Ribonuclease P RNA Conjugates
AUTHOR(S): Frank, Daniel N.; Harris, Michael E.; Pace, Norman R.
CORPORATE SOURCE: Department of Biology, Indiana University, Bloomington, IN, 47405, USA
SOURCE: Biochemistry (**1994**), 33(35), 10800-8
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB RNase P generates the mature 5' end of tRNAs by removing 5' leader sequences from pre-tRNAs. In vitro, the RNA subunit is sufficient to catalyze this reaction and is therefore a ribozyme. The kinetic anal. of RNase P-mediated catalysis is complicated because product release is normally rate-limiting. Furthermore, the intermol. nature of the cleavage reaction precludes many applications of in vitro selection schemes to the anal. of RNase P. To examine and manipulate the RNase P function more effectively, the authors designed a pair of ribozymes in which the RNase P RNA is covalently linked to a pre-tRNA substrate. To facilitate intramol. cleavage, pre-tRNA mols. were tethered to circularly permuted RNase P RNA mols. at nucleotides implicated in substrate binding. These "active-site-tethered" pre-tRNA-RNase P RNA conjugates undergo accurate and efficient self-cleavage in vitro, with first-order reaction rates equivalent to the rate of the chemical step of the native RNase P reaction. Unlike most ribozymes, RNase P recognizes its substrate through tertiary RNA-RNA interactions, rather than through extensive Watson-Crick base-pairing. However, the development of the active-site-tethered conjugates has led the authors to create a sequence-specific endonuclease, termed Endo.P. In the Endo.P configuration, the 3' half of the pre-tRNA acceptor stem binds exogenous RNA substrates via Watson-Crick base-pairing; the bound substrate is subsequently cleaved at the predicted site. The demonstration of sequence-specific cleavage by Endo.P expands the potential of RNase P and its derivs. as reagents in gene therapy.